IN THE CLAIMS:

Please substitute currently amended claim numbers 37 and 74 for the original or previously presented claims having the same claim numbers.

Please add new claims 75-80 for consideration.

1. (withdrawn) A method for detecting the presence or activity of a translocation promoting agent, wherein said translocation promoting agent is measured by:

(a) contacting a biological sample from a mammal in which the presence or activity of said translocation promoting agent is suspected with a binding partner of said translocation promoting agent under conditions that allow binding of said translocation promoting agent to said binding partner to occur; and

(b) detecting whether binding has occurred between said translocation promoting agent from said sample and the binding partner; wherein the detection of binding indicates the presence or activity of said translocation promoting agent in said sample; wherein said translocation promoting agent being capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

2. (withdrawn) A method for detecting the presence and activity of a polypeptide ligand associated with a given invasive stimulus in mammals comprising detecting the presence or activity of a translocation promoting agent according to the method of Claim 1, wherein

detection of the presence or activity of the translocation promoting agent indicates the presence and activity of a polypeptide ligand associated with a given invasive stimulus in mammals.

3. (withdrawn) The method of Claim 1 wherein said intracellular signal results in an increase in levels of intracellular calcium.

4. (withdrawn) The method of Claim 1 wherein said translocation promoting agent is a member of the transmembrane G-protein coupled receptor family.

5. (withdrawn) The method of Claim 1 wherein said translocation promoting agent is derived from a human cell.

6. (withdrawn) The method of Claim 5 wherein the translocation promoting agent is CC-CKR5.

7.(withdrawn) A method for identifying a viral envelope glycoprotein that binds a translocation promoting agent, comprising:

(a) contacting a labeled translocation promoting agent with a viral envelope glycoprotein attached to a solid support;

(b) washing the solid support; and

(c) detecting the labeled translocation promoting agent associated with the solid support; wherein a viral envelope glycoprotein that binds a translocation promoting agent is identified when the labeled translocation promoting agent is detected associated with the solid support; wherein said translocation promoting agent is capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

8. (withdrawn) The method of Claim 7, wherein the viral envelope glycoprotein is an HIV envelope glycoprotein.

9. (withdrawn) The method of Claim 7, wherein the translocation promoting agent is CC-CKR5.

10. (withdrawn) An assay system for screening a drug for its ability to modulate the production of a translocation promoting agent, comprising:

(a) culturing a mammalian cell that has been inoculated with a drug;

(b) harvesting a supernatant from said cell; and

(c) examining said supernatant for the presence of said translocation promoting agent wherein an increase or a decrease in a level of said translocation promoting agent indicates the ability of the drug to modulate the activity of said translocation promoting agent, said translocation promoting agent capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

11. (withdrawn) A test kit for the demonstrating the presence of a translocation promoting agent in a eukaryotic cell, comprising:

(a) a predetermined amount of a detectably labeled specific binding partner of a translocation promoting agent;

(b) other reagents; and

(c) directions for use of said kit; wherein said translocation promoting agent is capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

12. (withdrawn) The test kit of Claim 11 further comprising a predetermined amount of a translocation promoting agent.

13. (withdrawn) The test kit of Claim 11 wherein said detectably labeled specific binding partner of a translocation promoting agent is selected from the group consisting of polyclonal antibodies to the translocation promoting agent, monoclonal antibodies to the translocation promoting agent, fragments thereof, and mixtures thereof.

14. (withdrawn) A method of preventing and/or treating cellular debilitations, derangements and/or dysfunctions and/or other disease states in mammals, comprising administering to a mammal a therapeutically effective amount of a material selected from the group consisting of an agent capable of inhibiting the production of a translocation promoting agent, soluble translocation promoting agent, antagonists to said translocation promoting agent, cognates

thereof, fragments thereof, and mixtures thereof, or a specific binding partner thereto, said translocation promoting agent capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

15. (withdrawn) The method of Claim 14 wherein said disease states include AIDS, and related conditions.

16. (withdrawn) The method of Claim 14 wherein said intracellular signal results in an increase in levels of intracellular calcium.

17. (withdrawn) The method of Claim 14 wherein said translocation promoting agent is a member of the transmembrane G-protein coupled receptor family.

18. (withdrawn) The method of Claim 14 wherein said translocation promoting agent is CC-CKR5.

19. (withdrawn) A pharmaceutical composition for the treatment of cellular debilitation, derangement and/or dysfunction in mammals, comprising:

(a) a therapeutically effective amount of a material selected from the group consisting of an agent capable of inhibiting the production of a translocation promoting agent, soluble

translocation promoting agent, antagonists to said translocation promoting agent, cognates thereof, fragments thereof, and mixtures thereof, or a specific binding partner thereto; and

(b) a pharmaceutically acceptable carrier; wherein said translocation promoting agent is capable of promoting the translocation of macrophage-tropic virus through the membrane of a target $CD4^+$ cell, said translocation promoting agent comprising a material selected from the group consisting of a protein, active fragments thereof, agonists thereof, mimics thereof, and combinations thereof, said translocation promoting agent having the following characteristics:

(i) the agent is present in or on or proximal to the cell membrane of said target cell;

(ii) the agent acts in conjunction with CD4 in connection to said translocation; and

(iii) the agent is in association with a G-protein, wherein said association can facilitate an intracellular signal.

20. (withdrawn) The composition of Claim 19 wherein said translocation promoting agent is a member of the transmembrane G-protein coupled receptor family.

21. (withdrawn) The composition of Claim 20 wherein said translocation promoting agent is CC-CKR5.

22. (withdrawn) A transgenic non-human mammal comprising a DNA construct containing a human CD4 gene and a DNA construct containing human CC-CKR-5 gene wherein both CD4 protein and CC-CKR-5 protein are expressed by said non-human mammal.

23. (withdrawn) The transgenic non-human mammal of Claim 22, wherein the DNA construct for the human CD4 gene contains a T cell-specific transcriptional enhancer element.

24. (withdrawn) The transgenic non-human mammal of Claim 22, wherein said non-human mammal is a mouse.

25. (withdrawn) The transgenic non-human mammal of Claim 24, wherein said mouse lacks endogenous CD4.

26. (withdrawn) The transgenic non-human mammal of Claim 25 wherein said lack of endogenous CD4 is due to selective inactivation of the CD4 gene by gene targeting.

27. (canceled)

28. (canceled)

29. (canceled)

30. (canceled)

31. (canceled)

32. (canceled)

33. (withdrawn) A cell that is transfected with CD4 and a mimic of the translocation promoter agent wherein both CD4 and the translocation promoting agent are expressed by said cell, and said mimic has the ability to function with CD4 and permit entry into a cell of a virus pseudotyped with a macrophage-tropic envelope; wherein said cell is measurably susceptible to infection by a virus pseudotyped with a macrophage-tropic envelope; and wherein said mimic is a truncated chemokine receptor or a small organic molecule.

34. (withdrawn) An antisense nucleic acid against an mRNA coding for CC-CKR5 comprising a nucleic acid sequence that hybridizes to said mRNA.

35. (withdrawn) A recombinant DNA molecule having a DNA sequence which, on transcription, produces the antisense nucleic acid of Claim 34.

36. (withdrawn) A cell line transfected with the recombinant DNA molecule of Claim 35.

37. (currently amended) A method ~~for selecting for~~ of identifying an agent ~~for possible use in the treatment of an HIV infection caused by~~ that inhibits entry of a macrophage-tropic HIV virus into a target cell, wherein ~~fusion~~ entry of the macrophage-tropic HIV virus to said target cells is a fusion process mediated by CCR5 and CD4 expressed on the surface of said target cell, the method comprising the steps of:

(a) contacting ~~an agent with a~~ said cell ~~in the presence of~~ with a macrophage-tropic HIV virus or a virus pseudotyped with a macrophage-tropic HIV envelope~~; wherein in the absence of the agent said cell undergoes fusion with the macrophage-tropic HIV virus or the virus pseudotyped with a macrophage-tropic envelope; wherein CCR5 and CD4 are components of the surface of said cell; and wherein said fusion is mediated by CCR5~~ in the presence or absence of said agent;

(b) measuring the ~~ability of said cell to resist~~ fusion ~~with~~ between the macrophage-tropic HIV virus or the virus pseudotyped with a macrophage-tropic HIV envelope and said target cell; wherein fusion is measured by a method selected from the group consisting of visual (microscopic) assessment of syncytia formation, measurement of reporter gene expression and measurement by fluorescence activated cell sorting (FACS), and

(c) ~~selecting the agent when the measured ability of said cell to resist~~ determining whether fusion ~~with~~ of the macrophage-tropic HIV virus or the virus pseudotyped with a macrophage-tropic HIV envelope is ~~statistically greater~~ inhibited in the presence of the agent ~~than~~ but not in the absence of the agent.

38. (withdrawn) An assay for selecting a plausible therapeutic agent for possible use in the treatment of AIDS with the use of the transgenic non-human mammal of Claim 22, comprising:

(a) administering a suspected therapeutic agent to the transgenic non-human mammal;

(b) infecting said transgenic non-human mammal with a virus pseudotyped with a macrophage-tropic envelope;

(c) measuring the ability of said transgenic non-human mammal to resist said infection; and

(d) selecting the suspected therapeutic agent when the measured ability of said transgenic mammal to resist said infection is statistically greater in the presence of said suspected therapeutic agent than in the absence of said suspected therapeutic agent; wherein said selected suspected therapeutic agent is a plausible therapeutic agent.

39. (withdrawn) A method of filtering a biological fluid to remove a virus pseudotyped with a macrophage-tropic envelope wherein the biological fluid is passed through the cell of Claim 29.

40. (withdrawn) The method of Claim 39 when said biological fluid is selected from the group consisting of blood, semen, and cerebrospinal fluid.

41. (canceled)

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60. (canceled)

61. (withdrawn) A nucleic acid encoding a chimeric translocation promoting agent, wherein the chimeric translocation promoting agent is a chemokine receptor having an epitope tag in its amino-terminal extracellular domain.

62. (withdrawn) A nucleic acid of claim 61, wherein the chemokine receptor is CC-CKR5.

63. (withdrawn) A nucleic acid of claim 62, wherein the chimeric translocation promoting agent comprises the amino acid sequence of SEQ ID NO:6 in its amino-terminal extracellular domain.

64. (withdrawn) An expression vector comprising the nucleic acid of Claim 61.

65. (withdrawn) The expression vector of Claim 64, wherein the nucleic acid encodes a chimeric translocation promoting agent comprising the chemokine receptor CC-CKR5 having an amino acid sequence of SEQ ID NO:6 in its amino-terminal extracellular domain.

66. (withdrawn) A method of making an identifiable cell that has the chimeric translocation promoting agent in its cell membrane comprising:

(a) transfecting a cell with the expression vector of Claim 64; and

(b) detecting the epitope tag with an antibody that recognizes the epitope tag; wherein said detecting identifies the cell as having the chimeric translocation promoting agent in its cell membrane.

67. (withdrawn) The method of Claim 66, wherein the chemokine receptor is CC-CKR5 comprising an amino acid sequence of SEQ ID NO:6 in its amino-terminal extracellular domain; and wherein the antibody is anti-influenza (HA) monoclonal antibody.

68. (withdrawn) A chimeric translocation promoting agent comprising a chemokine receptor having an epitope tag in its amino-terminal extracellular domain.

69. (withdrawn) The chimeric translocation promoting agent of Claim 68, wherein the chemokine receptor is CC-CKR5 comprising an amino acid sequence of SEQ ID NO:6 in its amino-terminal extracellular domain.

70. (previously presented) The method of Claim 37 wherein the method further comprises:

(d) contacting the agent with CCR5; and

(e) determining if the agent binds to CCR5; wherein an agent that binds CCR5 is selected; and wherein steps (d) and (e) can be performed either prior to or after steps (a)-(c).

71. (withdrawn) An antibody that is specific for an epitope of CCR5 that becomes accessible upon the binding of CCR5 with CD4 and/or an envelope protein of HIV-1.

72. (withdrawn) An antibody that reacts with a shared epitope, wherein the shared epitope is formed by CCR5 binding an envelope protein of HIV-1, and/or CD4.

73. (withdrawn) The antibody of Claim 72 that is a chimeric antibody.

74. (currently amended) A method ~~for selecting for~~ of identifying an agent ~~for possible use in the treatment of an HIV infection caused by~~ that inhibits entry of a macrophage-tropic HIV virus into a target cell, wherein entry of the macrophage-tropic HIV virus into ~~cells~~ said target cell is a fusion process mediated by CCR5 and CD4 expressed on the surface of said target cell, the method comprising the steps of:

(a) contacting ~~an agent with a~~ said cell ~~in the presence of~~ with a macrophage-tropic HIV virus or a virus pseudotyped with a macrophage-tropic HIV envelope~~; wherein in the absence of the agent said cell undergoes fusion with and/or permits entry to the macrophage-tropic HIV virus or the virus pseudotyped with a macrophage-tropic envelope; wherein CCR5 and CD4 are components of the surface of said cell; and wherein said fusion or entry is mediated by CCR5~~ in the presence or absence of said agent;

(b) measuring the ~~ability of said cell to resist~~ fusion ~~with and/or permit entry~~ between ~~to~~ the macrophage-tropic HIV virus or the virus pseudotyped with a macrophage-tropic HIV envelope and said target cell, wherein fusion is measured by a method selected from the group consisting of visual (microscopic) assessment of syncytia formation, measurement of reporter gene expression and measurement of fluorescence activated cell sorting (FACS); and

(c) ~~selecting the agent when the measured ability of said cell to resist~~ determining whether fusion ~~with and/or entry to~~ of the macrophage-tropic HIV virus or the virus pseudotyped

with a macrophage-tropic HIV envelope is ~~statistically greater~~ inhibited in the presence of the agent ~~than~~ but not in the absence of the agent;

(d) contacting the agent with CCR5; and

(e) determining if the agent binds to CCR5; wherein an agent that binds CCR5 is selected; and wherein steps (d) and (e) can be performed either prior to or after steps (a)-(c).

75. (new) The method of claim 37, wherein said target cell is a transformed mammalian cell that:

(d) contains a gene encoding CD4;

(e) contains a construct encoding a reporter gene under the regulation of an HIV LTR; and

(f) that has been transduced with a vector encoding a human chemokine receptor; wherein CD4 and the human chemokine receptor are present on the surface of the cell.

76. (new) The method of claim 75, wherein the vector is a retroviral vector.

77. (new) The method of claim 75, wherein the cell is a human cell.

78. (new) The method of claim 77, wherein the human cell is HOS.CD4 having the ATCC Accession Number PTA-1916.

79. (new) The method of claim 75, wherein the reporter gene encodes green fluorescent protein.

80. (new) The method of claim 75, wherein the HIV LTR is HIV-2 LTR.